a failure to provide productive occupations help to keep up the symptoms. I have seen hysterical paraplegics who had been bedridden in surgical wards for a couple of months, chop down trees a few days after coming to the neuropsychiatric wards. The will to work is very important. It is self-evident that the loss of the work habit is disastrous. The wish to be cured is essential. A careful and systematic examination makes an impression on these patients; it therefore has therapeutic value. The patient must be made to realize his obligations. Any asocial tendencies, as well as hypochondriacal trends, must be combated. Do not allow the patient to develop an attitude of chronic invalidism. Treat the patient and his disordered personality: they are of greater importance than the symptoms.

The reëducation of the patient must not be confined to a mere restoration of his lost physical function, but must also include the correction of any defects of feeling, will or intellect.

Electricity and massage are used almost entirely for their suggestive influence. Any concomitant physical disorder must be treated according to the dictates of rational medicine.

A very important point to remember is that one's self-assurance of success has greater effect on the patient than any direct reasoning one may employ. This is nothing new, but physicians often disregard this dictum, and we see neurotic patients frequently going to various frauds and quacks who succeed just because they apply this point with emphasis. The hypersuggestible patients have full faith in the assurances.

The neuroses of war have taught us but little that is new. But because of their frequency and the widespread interest that has been taken in them they will probably stimulate physicians in the future to take a greater interest in the neuroses of civil life.

LOCALIZATION OF TUMOR METASTASES.

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The term metastasis as applied to tumors is generally held to mean generalization of a growth by formation of secondary deposits throughout various tissues and organs of the body and not directly connected with each other. But this is really not an all-embracing

definition, for the conception of metastasis requires not only deposit, but subsequent growth of the misplaced tumor cells, with replacement of the physiological tissue by the tumor. Thus all kinds of cells, including bacteria, may become dislodged from their original focus and be arrested in different situations, but we can only speak of a metastasis when this new location is involved by disease; for the passive lodgment of foreign cells may be, and frequently is, followed by their destruction or quiescence. The appearance of foreign cells in an organ or tissue is therefore significant and practically important as a step toward metastasis, but in itself is not proof of it.

This important point has not received adequate consideration in recent experimental work on the artificial production of cancer. The fact that, on artificial stimulation by lipoid solvents and other irritatants, proliferation of cells has occurred and that some of these newly formed cells have been disconnected and have reached neighboring tissues and even lymph glands by means of the lymph stream, is no proof of their metastasizing quality or even true tumor character. This proof is furnished only then when it can be demonstrated that these cells are not only carried by a stream and arrested in a tissue, but possess the ability of growth and organization to a tumor and the power of replacement of the physiological tissue.

The same strict interpretation of metastasis must be applied to spontaneous tumors. If, for example, we find on microscopic examination tumor cells arrested in the capillaries of the lung which they have reached by a massive break of a growth into the venous system, we are not really justified to speak of a metastasis in the lung, although that is often enough done. In infections the evidence of the disease is the anatomical lesion. Just so, in tumor metastasis the evidence is growth of tumor tissue into and annihilation of physiological tissue by it.

Emphasis is put on this point not only because of the previously stated erroneous interpretation placed on the appearance of arrested, disconnected cells in experimental cancer production in animals, but because an investigation into the problems of tumor metastases is rendered impossible by lumping the occurrence of tumor emboli with actual growth of tumor cells; for the problem of tumor metastases is not to be found in the transport and arrest of cells but in their growth to a tumor tissue. Upon this depends the unique encroachment and replacement of physiological tissue, which are the genuine attributes of metastasis.

One other point is not sufficiently appreciated, especially by clinicians, and needs explanation at the start. It is generally assumed that the histological picture is an almost absolute expression of the biological character of a growth; in other words, that malignancy and formation of metastases go hand-in-hand with the

immaturity of tumor components, that tumors of embryonic undifferentiated parenchyma are malignant and metastasizing and tumors of mature cells and arrangement benign and local.

A more profound consideration of this statement will show that this idea is untenable and cannot be upheld as a general law of tumor growth; for we know a number of tumors of embryonic tissue which do not, or at least very rarely, generalize. These are the sarcogliomata; congenital melanomata (nevi); spindle-cell sarcomata or endotheliomata of the dura mater; the epulis; many sarcomata and cancers of the ovary, of the uterus and of the mediastinum; sarcomata of the fascia; the teratomata and the embryonic growths or remains of the gut and the appendix. These tumor types may exist for years, are often an accidental finding, and do not, except in rare instances, exhibit any tendency to infiltrate and metastasize, although they may locally recur after excision.

On the other hand the reverse is also true, for anatomically mature so-called benign tumors will occasionally lead to secondary growths. This now well-established fact has been observed in fibromata, myxomata, lipomata, gliomata of the retina, angiomata, enchondromata, myomata and typical thyroid tumors.

This interesting and practically important fact was already well known to Virchow, but especially emphasized in the brilliant discussion of tumor growth by Cohnheim in his lectures on general pathology. So much were Virchow and Cohnheim impressed by these observations that the former believed that malignant properties in a tumor were subsequent to an innocent period, and Cohnheim, going further, advanced the view that malignancy and power of metastasis were in no way dependent upon the nature of the growth. To the contrary it was his opinion that infiltration and metastases depended upon the condition of the surrounding tissue. Cohnheim, following the reasoning of Thiersch on the primary development of cancer, attributed the occurrence of metastases to a removal of the physiological resistance in the invaded tissue. He attempted to support this idea experimentally by artificial introduction of periosteal flaps into the pulmonary circulation through the jugular vein. He and Maas observed in such cases the formation of thrombi of periosteal tissue. Within two weeks occurred growth of periosteal cells in these vessels to cartilage and bone. Then, however, they regressed, did not invade the neighboring tissue and finally succumbed. The conclusions which Cohnheim drew from these and similar observations of Goldtzieher and Schweninger were that regression occurred because the foreign cells were unable to resist the metabolism of the physiological tissue. Consequently, Cohnheim applied these ideas to the problem of metastases: "Only when and where tissues are lowered in their physiological matabolism by age, atrophy and inflammation will metastases be possible."

A study of tumor metastases carried on in a series of ninety-eight

successive cases of metatasizing tumors of various kinds and derivation in the laboratories of the Royal Victoria Hospital and of McGill University has revealed that in the localization of metastases two determining factors exist, viz., quantity and quality of tumor cells. It appears that in these respects tumor cells may be compared to invading parasites. In one as in the other instance the manner of invasion as well as the quantity introduced are naturally of great importance. It may be compared to the well-known difference of tuberculous infection, in which much depends upon how and how many tubercle bacilli invade an organism. When ordinarily a relatively small number are introduced and moved along by the lymph stream, they are anchored by certain tissues more readily than by others, and it is well known that the lungs, quite apart from mechanical considerations, are most susceptible to the insults of this microörganism.

On the other hand, when tubercle bacilli are poured in large quantities directly into the blood stream or even lymph stream such an elective action and localization do not occur and disseminated miliary tuberculosis develops in practically all organs of the body.

The first instance illustrates qualitative selection, the second simply quantitative overwhelming of the body by the infecting agent.

Similar conditions are found to prevail in the manner and method of some tumor metastases. In a case of small prostatic cancer, so small that only microscopic examination revealed it, practically all organs of the body were the seat of small, nodular, multiple metastases, closely resembling miliary tubercles, and clinically the case had been diagnosed as miliary tuberculosis. Careful microscopic examination of this prostate showed an unusual rupture of small tumor cells into small veins of the prostate, and from these the generalization had probably occurred.

A similar generalization is more frequently seen in the so-called hypernephromata or renal cancers. Here our laboratory records show a not infrequent massive rupture of softened tumor masses into the renal vein and extension *en masse* to the right heart and lung. In one case of a male, aged fifty-four years, a tumor thrombus extended from the right renal vein through the vena cava and the right auricle into the right ventricle and, apparently following the blood current, into the pulmonary artery. The smallest branches of this artery showed tumor emboli and, simulating miliary tuberculosis, small tumor growths in the parenchyma around them. Similar tumor plugs were found in the iliac veins and metastases in the liver and spleen.

These and other cases illustrate that even cancers may travel by the blood stream and that this path of dissemination, together with a large quantity of tumor cells thus introduced, dictates the distribution of the metastases.

Turning now to the frequent metastases in the regionary glands in close proximity with a tumor, several factors must be considered.

In the first place it is practically important that not all enlarged glands in the neighborhood of tumors are the seat of metastases. They are frequently simply inflammatory enlargements. It may be said that this is the rule in the enlargement of the pelvic glands in cancer of the uterus and in the lymph glands of the neck in cancer of the tongue, and is even frequently seen in the portal glands and mesenteric glands in cancer of the stomach and the gut. Sometimes these glands remain inflammatory throughout the course of the tumor growth; in other cases, however, they become sooner or later the seat of metastases. In a case of an extensive squamous-cell cancer at the base of the right side of the tongue, recently observed, the submaxillary lymph glands on both sides were distinctly enlarged and firm. On the left side they proved to be, on microscopic examination, only inflammatory; on the right side several of them showed small, early metastases taking origin from the lymph sinuses.

The relationship of the inflammatory changes to the tumor metastases is instructive and suggestive. It is not impossible that at least in a number of these cases, in which infection by bacteria can be reasonably excluded the constant drain of metabolic tumor products is irritating to the gland tissue, and thus, by lasting injury and upset of physiological tissue balance by inflammatory changes, predisposes the organ to metastatic growth. If this is the case it would appear to have an important bearing on the formation of metastases; for it would indicate that, under certain conditions at least, the occurrence of metastases is made possible or favored by a drain of metabolic tumor products into a tissue.

Cohnheim's theory may therefore be correct in emphasizing lack of resistance on the part of the physiological tissue and inability to dispose of these foreign cells. This weakening of the physiological tissue may, moreover, be due to the direct action of specific tumor products. This theory would naturally apply best to the explanation of those metastases which are nearest and most intimately connected with the original growth and in which a more or less constant and concentrated communication exists. Late metastases might be explained by gradual weakening of physiological resistance.

But when we come to distant, often isolated metastases and consider the frequency with which some organs are involved in certain types of tumors irrespective of their primary location it is evident that other factors must enter into their formation.

Mechanical arrest of tumor plugs through anatomical peculiarities can hardly be of paramount importance in such cases, for everyone knows how rarely the spleen is the seat of a secondary tumor. By virtue of its anatomical structure as a true filter it offers the best

mechanical arrangement for detention of tumor cells. There must, therefore, exist other reasons.

Virchow drew attention to the fact that those organs which are rarely the seat of primary tumors are the most chosen seat for secondary deposits. This, however, can hardly be generalized, and Virchow, himself, gave no explanation of the matter.

In order to arrive at a knowledge of the frequency with which certain tissues are selected in metastases an analysis of the ninety-eight cases studied in this laboratory during the last few years was made. The malignant tumors were first classified according to their ordinary histological appearance. Then their embryogenetic origin was determined, that is, from which layer of the blastoderm the growth originated. The location of the metastases was then analyzed according to the occurrence of metastases in ectodermal, mesodermal and entodermal tissue. The glands were analyzed by themselves.

Type of tumor.		Location of metastases. Ectoderm.	Mesoderm.	Entoderm.	Glands.
Epitheliomata,	11	0	2	2	8
Adenocarcinomata,	29	2	16	20	16
Carcinomata,	36	5	13	30	20
Sarcomata,	7	0	6	8	10
Endotheliomata,	6	0	3	6	8
Teratomata	1	0	2	1	0

CHART I

Type of tumor.	Origin of tumor.	Ectoderm.	Location of metastases. Mesoderm.	Entoderm.	Glands.
Epitheliomata	3 Ectoderm	0	1	0	2
	8 Entoderm	0	1	2	6
Adenocarcinomata	2 Ectoderm	0	5	4	3
	5 Mesoderm	1	3	2	1
	22 Entoderm	1	8	14	12
Carcinomata	3 Ectoderm	4	4	5	1
	4 Mesoderm	0	2	2	2
	29 Entoderm	1	7	23	17
Sarcomata	1 Ectoderm	0	1	0	1
	5 Mesoderm	0	5	8	9
	1 Entoterm	0	0	0	0
Endotheliomata	6 Mesothel	0	3	6	8
Teratomata	1	0	2	1	0

CHART II

It is, of course, impossible to draw from such a table definite conclusions regarding the selective property of metastases, for other factors but selective action, some of which have previously been mentioned, complicate the value of such charts. Nevertheless, some points are interesting and more or less suggestive. Thus it will be seen that of 22 adenocarcinomata which took their origin from entoderm, 14 metastases formed in entoderm, and of 29 carcinomata which were derived from entoderm, 23 formed metastases in entoderm. Furthermore, of 5 sarcomata, 5 metastases occurred in mesodermal tissue. It is true that in these sarcomata there were

also 8 metastases in entoderm organs—the liver, the lungs and the pancreas—but the metastases in these instances were apparently not selective but due to causes previously discussed. It is also not unlikely that selection is greater in growths derived from more highly differentiated entodermal glandular tissue.

Although the material analyzed is relatively small a suggestion is contained in it that embyrogenetic and biological relationship of tumor tissue to physiological tissues may influence the often strange selective metastases. In other words it would appear as if close embryogenetic affinity of tumor cells to tissues of the same derivation influence metastatic selection. It is well known that lymphosarcomata metastasize with preference in lymphadenoid or mesodermal tissues.

The conclusion is therefore reached that the localization of metastases depends upon a number of factors. Important among these are:

1. The quantity of the tumor elements and the method of dissemination.

2. Effects of injurious metabolic products of tumor cells upon a tissue, causing degeneration and inflammation and thereby weakening its physiological resistance.

3. Close biogenetic (embryonic) relation of tumor cells to a tissue soil, whereby types of tumor cells derived from an embryonic layer grow more readily in the environment of organs or tissues which are derived from the same layer of the blastoderm.

Accurate determination of this last point will only be possible with a large amount of tumor material analyzed grossly and microscopically with full regard to the factors discussed above.

ISOLATION OF THE MENINGOCOCCUS FROM CASES OF SO-CALLED INFLUENZA.

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AND

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INTRODUCTION. Material for the following bacteriological study was obtained from cases occurring in two epidemics of so-called influenza and from a number of scattered cases admitted to the U. S. Base Hospital No. 6, Bordeaux, France. The first epidemic spread among a forestry organization stationed in and about Mimizan in the Department of Landes. In the three camps affected,